REMARKS

Claims 1-7 and 10-21 are pending the application; Claims 1-7 and 10-21 stand rejected. By this Amendment Claims have been 1-3, 6-7 and 14 are canceled and Claims 4, 5, 10-13 and 15-21 have been amended. New claims 22-27 are added. These amendments and new claims add no new matter to the application.

Claims 1-7 and 10-21 stand rejected un 35 USC 112 as allegedly not enabled for the skilled artisan's use without undue experimentation; Applicant respectfully traverses these rejections. Rejections of Claims 1-3 and 6-7 are moot in view of the cancellation of Claims 1-3 and 6-7; rejections of Claims 13-21 are particularly traversed in that the operative claim terms upon which the Examiner focuses the 'undue experimentation' argument is the term 'derivative', and Claims 13-21 make no use of that term.

Applicant again asserts that there is no authority for the Examiner's reliance on a supposed lack of working examples as to how any of the other claimed embodiments may be employed in the claimed methods. The method claims at issue all clearly state their mode of employment, and no experimentation at all is required to practice the invention as variously claimed, it being well accepted by those skilled in the art that determination of appropriate therapeutically effective amounts of claimed compositions is not considered to be experimentation. This is particularly true when, as is presented in this case, the efficacy of the disclosed embodiments is so great in general as to render practically any amount of any of the disclosed embodiments at least minimally therapeutically effective.

Applicant respectfully submits that the Examiner' citation to *In re Wands* is not appropriate as authority for the Examiner's assertion that working examples are required. In fact, working examples, even according to the cited case, are only <u>one</u> out of eight listed factors to consider in

the determination of whether undue experimentation might be required. In this case where no experimentation at all, or virtually none, is needed to deliver therapeutic efficacy for the disclosed compounds, it is simply insufficient as a matter of law to cite the *In re Wands* factors, as if an application missing even one of the listed eight factors were automatically defective in that regard. The most the Examiner may legally infer from the citation is that the presence of more working examples might be considered helpful, but not required.

Neither does the Examiner's generalized statement that 'the pharmaceutical art is unpredictable' serve as adequate legal authority for an automatic 'undue experimentation' rejection. In fact, persons skilled in the art agree that the pharmaceutical art is not uniformly unpredictable; and in this case, the predictability of therapeutic efficacy is great.

Applicant alone has originally discovered and disclosed for the public benefit the efficacy of the various disclosed substances all for treating amyloidoses, and amyloid and alpha-synuclein fibrillogenesis, and alone is entitled under the law to claims of commensurate scope with this discovery and disclosure. It is after all the policy underlying the law, and the very constitutional provision for patents itself, that the public be bettered by so encouraging just this kind of discovery and disclosure with the issuance of patent grants.

The term 'derivative' has been removed from remaining Claims 4, 11 and 12, which, apart from now canceled claims 1-3 and 6-7 are the only claims formerly making use of the term. This rejection is thus moot as to claims 4, 11 and 12 as well. In addition, it is well known that it is not necessary for the skilled artisan to be able to come up with every possible compound that might be covered by the limitations of a claim; it being sufficient if the artisan is shown a single example of the species covered, and the *Fisher* case cited is not to the contrary. Therefore the remaining

claims are allowable and Applicant requests reconsideration of the rejected claims in light of the above arguments.

Claims 1-5 and 10-21 stand rejected un 35 USC 112 as allegedly indefinite; Applicant respectfully traverses these rejections. Applicant asserts that the term 'standardized green tea extract' is well known in the art, but in the interests of early indication of allowable subject matter, the word 'standardized' is removed. Applicant asserts that 'age-associated' and 'age-related' in Claim 18 are definite in their usage, as is well understood in the pathological arts to which the claim is related.

The terms 'age-related' and 'age-related' occur only in claims 18 and 19, and therefore this rejection is particularly traversed for every other claim in the case. In particular it is well known that certain "brain or cognitive disorders" are "age-related"; it is submitted therefore that there is no indefiniteness in the term 'age-related.' Similarly, the term 'age-associated' is likewise a well known construction in the context of discussing various pathologies of the brain. The rejected claims are therefore allowable and reconsideration is requested.

Claims 1-4 and 10-11 stand rejected under 35 USC §102 as allegedly anticipated by Castillo WO 98/51302; Applicant respectfully traverses these rejections. Amended claims 4 and 11 now require administering epicatechin, bioflavanoids, flavanols, flavandiols, flavanoids, or tannins; Castillo does not make any mention of these compounds as efficacious in anti-fibrillogenesis. Castillo thus does not anticipate claims 1, 4 or 11. Claim 10 depends from claim 1 and properly construed contains all the limitation of claim 1, and is therefore not anticipated either. These claims are all believed to be allowable over Castillo, and reconsideration is requested.

Claims 1-4 stand rejected under 35 USC §102 as allegedly anticipated by JP 10245342 (Mitsui Norin); Applicant respectfully traverses these rejections. Claim 1 is canceled and Claim 4 now requires administering a therapeutic amount of epicatechin, bioflavanoids, flavanols, flavandiols, flavanoids, or tannins to a subject to treat amyloid fibril formation. Mitsui Norin does not make any mention of fibril formation at all. Mitsui Norin teaches narrowly only that nerve cell toxicity supposedly caused by beta-amyloid protein may be reduced with tea polyphenols; the reference makes no suggestion about treatment or reduction of amyloid fibril formation, or disruption/disassembly of pre-formed amyloid fibrils at all. Applicant on the other hand teaches and claims a method of use of disclosed substances to actually interfere with and prevent or reverse amyloid and alpha synuclein fibril and plaque formations. A general reference to tea polyphenols is not a teaching of the efficacy of specific polyphenols. Claim 4 therefore does not read upon any teaching or suggestion by Mitsui Norin. Mitsui Norin's teaching is also not inherent in method claim 4, since the cited doctrine of inherency does not apply to method claims. The specific limitations of Claim 4 must be read in any attempt to read it upon any prior art methods, and the claimed method differs from the Mitsui Norin teachings. These claims are all believed to be allowable over Mitsui Norin, and reconsideration is requested.

Claims 1-9 and 11-12 stand rejected under 35 USC §102 as allegedly anticipated by Shin-ya; Applicant respectfully traverses these rejections. Claim 4 now requires administering a administering a therapeutic amount of epicatechin, bioflavanoids, flavanols, flavandiols, flavanoids, or tannins to a subject to treat amyloid fibril formation. Claim 11 has always been addressed to Parkinson's disease and Lewy body formation and alpha synuclein fibril formation. Shin-ya makes no mention of amyloid fibril formation, or disruption/disassembly of pre-formed amyloid fibrils at all, and teaches nothing about Parkinson's disease and Lewy body formation and

alpha synuclein fibril formation. Shin-ya teaches only that nerve cell death induced by active oxygen and supposedly mediated by beta-amyloid protein may be reduced with catechin; the rejected claims therefore do not read upon any teaching or suggestion by Shin-ya, since the reference discusses only active oxygen induced nerve cell death. Shin-ya's teaching is also not inherent in the rejected claims and does not anticipate them. These claims are all believed to be allowable over Shin-ya and reconsideration is requested.

Claims 1-9 and 11-12 stand rejected under 35 USC §102 as allegedly anticipated by Schultes; Applicant respectfully traverses these rejections. Claim 4 now requires administering a administering a therapeutic amount of epicatechin, bioflavanoids, flavanols, flavandiols, flavanoids, or tannins to a subject to treat amyloid fibril formation. Claim 11 has always been addressed to Parkinson's disease and Lewy body formation and alpha synuclein fibril formation. Schultes makes no mention of amyloid fibril formation, or disruption/disassembly of pre-formed amyloid fibrils at all, and teaches nothing about Parkinson's disease and Lewy body formation and alpha synuclein fibril formation. Schultes deals narrowly only with certain naturally occurring cholinesterase inhibitors and the view that certain dementias like Alzheimer's might be susceptible to treatment with such inhibitors. The reference is concerned not at all with reduction of amyloid fibril formation. Applicant teaches and claims a method of use of disclosed substances to actually interfere with and prevent or reverse fibril and plaque formations. The rejected claims thus do not read upon any teaching or suggestion by Schultes and Schultes' teachings are not identical with the claimed method steps; they are therefore not inherent in the rejected claims and do not anticipate them. These claims are all believed to be allowable over Schultes and reconsideration is requested.

New claims 22-27 are added at this time as composition of matter claims corresponding to the respective method claims already in the case. It is believed that no new searching will be required for these new claims.

Applicant has asked that the listing of inventors in the application be corrected such that Castillo is the first inventor listed, all in accordance with the original filing papers in this case filed 12/29/00, and not in accordance with subsequently issued filing receipts.

Applicant believes that he has responded fully to all of the concerns expressed by the Examiner in the Final Action, and respectfully requests that early favorable action be taken on all claims pending in the application. Applicant respectfully requests reexamination of all rejected claims and early favorable action on them as well. If the Examiner has any further concerns, Applicant requests a call to Applicant's attorney Patrick Dwyer at (206) 343-7074.

Respectfully submitted,

P16-RCE.RSP

PATRICK MICHAEL DWYER
Reg. No. 32,411

PATRICK M. DWYER
PROTEOTECH, INC.
1818 WESTLAKE AVENUE N, SUITE 114
SEATTLE, WA 98109

Amended Claims
(Version with Markings to Show Changes Made)

4. A method for the treatment, inhibition, prevention or management of amyloid fibril formation, deposition, accumulation, aggregation and/or persistence in Alzheimer's disease, type II diabetes and other amyloidoses in a mammalian subject, the method comprising the step of administering to the subject a therapeutic amount of a substance selected from the group of substances consisting of green tea, green tea leaves, ~~standardized~~ green tea extract, ~~green tea derivative,~~ epicatechin~~s~~, bioflavanoids, flavanols, flavandiols, flavanoids, and tannins ~~and well known derivatives of any of the foregoing substances~~.

5. The method of Claim 4, wherein the substance is ~~a catechin selected from the group of catechins consisting of catechin,~~ epicatechin~~, gallocatechin gallate, epigallocatechin gallate, epigallocatechin, and epicatechin gallate, or a derivative of one of the above group~~.

10. The method of Claim ~~1~~4 further comprising, in the step of administering ~~plant matter~~the therapeutic substance, additionally administering a therapeutic quantity of one or more plant materials selected from the group of plants consisting of, and commonly known as, Cat's claw, ginkgo biloba, rosemary, gotu kola, bacopin, and ginseng.

11. A method for the treatment, inhibition, prevention or management of α-synuclein fibril formation, deposition, accumulation, aggregation and/or persistence in Parkinson's disease or Lewy body disease in a mammalian subject, the method comprising the step of administering to the subject a therapeutic amount of a substance selected from the group of substances consisting of green tea, green tea leaves, ~~standardized~~ green tea extract, catechins, bioflavanoids, flavanols, flavandiols, flavanoids and tannins ~~and well known derivatives of any of the foregoing substances~~.

12. The method of Claim 11, wherein the substance is ~~a catechin selected from the group of catechins consisting of catechin,~~ epicatechin~~, gallocatechin gallate, epigallocatechin gallate, epigallocatechin, and epicatechin gallate, or a derivative of one of the above group~~.

13. A method for promoting mental alertness in a patient, the method comprising the step of administering to the patient a therapeutically effective amount of epicatechin~~plant matter from a plant of the family Theaceae~~.

~~14. The method of claim 13 wherein the plant matter comprises matter from a plant of the genus Camellia, species sinensis.~~

15. The method of claim 13 wherein the method is also for inhibiting the formation of brain amyloid deposits.

16. A method for promoting, maintaining or enhancing in a patient one or more of the mental or cognitive qualities selected from the group of mental or cognitive qualities consisting of mental acuity, mental alertness, cognitive well being, normal brain function, cognitive ability, mental performance, memory, concentration, mental sharpness, mental clarity, short term memory, normal brain function, and learning, the method comprising the step of administering to the patient a therapeutically effective amount of epicatechin~~plant matter from a plant of the genus Camellia, species sinensis~~.

17. A method for providing, supporting or improving in a patient one or more of the mental or cognitive qualities selected from the group of mental or cognitive qualities consisting of normal brain function, cognitive ability, and concentration, the method comprising the step of administering to the patient a therapeutically effective amount of epicatechin~~plant matter from a plant of the genus Camellia, species sinensis~~.

18. A method for reducing in a patient one or more of the mental or cognitive effects selected from the group of mental or cognitive effects consisting of, age-associated cognitive or memory decline, mental decline, and likelihood of age-related brain or cognitive disorders, the method comprising the step of administering to the patient a therapeutically effective amount of epicatechin~~plant matter from a plant of the genus Camellia, species sinensis~~.

19. A method for reducing, disrupting, dissolving, inhibiting, eliminating or preventing in a patient one or more conditions involving the brain selected from the group of conditions involving the brain consisting of amyloid fibril deposits, amyloid protein deposits, brain-associated amyloid fibril deposits, brain-associated amyloid protein deposits, amyloid fibril formation and growth, age-associated amyloid fibril formation and growth, brain-associated amyloid fibril formation and growth, the method comprising the step of administering to the patient a therapeutically effective amount of epicatechin~~plant matter from a plant of the genus Camellia, species sinensis~~.

20. A method for promoting or supporting healthy pancreatic function in a patient, by helping to promote normal insulin function, the method comprising the step of administering to the patient a therapeutically effective amount of epicatechin~~plant matter from a plant of the genus Camellia, species sinensis~~.

21. A method for reducing, disrupting, dissolving, inhibiting, eliminating or preventing in a patient one or more conditions involving the pancreas selected from the group of conditions involving the pancreas consisting of amyloid fibril deposits, amyloid protein deposits, pancreas associated amyloid fibril deposits, pancreas associated amyloid protein deposits, amyloid fibril formation and growth, pancreas associated amyloid fibril formation and growth, the method comprising the step of administering to the patient a therapeutically effective amount of epicatechin~~plant matter from a plant of the genus Camellia, species sinensis~~.